4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2013-N-0271]

Availability of Masked and De-identified Non-Summary Safety and Efficacy Data; Request for Comments

ACTION: Notice; request for comments.

AGENCY: Food and Drug Administration, HHS.

SUMMARY: The Food and Drug Administration (FDA) is seeking public comments from interested persons on the proposed availability of de-identified and masked data derived from medical product applications. Improving the efficiency and effectiveness of medical product development is a national priority. The ability to make available de-identified and masked clinical and preclinical data derived from marketing applications could make an important contribution to that goal by providing scientific data that may be of value in the generation of new knowledge to facilitate innovation in the development and evaluation of critically needed medical products. The contribution of patients who participate in clinical trials should be maximized for the benefit of society. The Agency invites comments on the issues to be considered with regard to such availability and on any limitations that should be placed on the availability of these data.

DATES: Submit either electronic or written comments by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration,

5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number found in brackets at the heading of this document.

FOR FURTHER INFORMATION CONTACT:

Nancy B. Sager,

Center for Drug Evaluation and Research,

Food and Drug Administration,

10001 New Hampshire Ave.,

HILL-3110,

Silver Spring, MD 20993,

301-796-3603,

FAX: 301-431-6351,

Nancy.sager@fda.hhs.gov; or

Stephen Ripley,

Center for Biologics Evaluation and Research (HFM-17),

Food and Drug Administration,

1401 Rockville Pike, suite 200N,

Rockville, MD 20852-1448,

301-827-6210; or

Aaliyah Eaves-Leanos,

Center for Devices and Radiological Health,

Food and Drug Administration,

10903 New Hampshire Ave.,

Bldg. 66, rm. 5435,

301-796-2948,

FAX: 301-847-8510.

Aaliyah.Eaves-Leanos@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

Commissioner of Food and Drugs Margaret Hamburg has emphasized FDA's role as a public health Agency (Ref. 1). In accordance with its responsibility to promote the public health, FDA has, in collaboration with the National Institutes of Health, launched the Regulatory Science Initiative, a call to action to enhance the science and knowledge critical to improving the development, manufacture, evaluation, and safe use of critically needed new therapies. In addition, the Food and Drug Administration Safety and Innovation Act (FDASIA), enacted on July 9, 2012, contains important new authorities that will enhance the Agency's ability to promote innovation across industry, research and clinical care settings, including new provisions that require the development of a plan for advancing regulatory science for medical products in order to promote the public health and advance innovation in regulatory decision making. (See, e.g., section 1124 of FDASIA (Public Law 112-144).)

The development of new knowledge and insights from clinical and preclinical study data is an important regulatory science opportunity. These data have a tremendous potential to help address critical challenges and provide new opportunities for innovation in medical product development, including for human drugs, medical devices, and biological products. Safety and effectiveness data from multiple studies have been used in the past to address key hurdles in drug development. Analysis of data from multiple clinical and preclinical studies has been used to identify potentially valid endpoints for clinical trials, understand the predictive value of

preclinical models, clarify how medical products work in different diseases, and inform development of novel clinical designs and endpoints to the benefit of patients.

For example, the primary endpoint for chronic hepatitis C trials has been based on detection of hepatitis C virus at week 24 of follow up. Evidence suggested that assessing the response at earlier follow up time points may provide an equivalent measurement of drug response. FDA scientists conducted an analysis of the combined data from 15 clinical trials and 3 pediatric trials from 5 drug development programs to determine whether assessments conducted at earlier time points could provide results that were predictive of the outcomes at 24 weeks of follow up (Ref. 2). The sustained virologic response measurements at 12 and 24 weeks of follow up were concordant across a large population database involving multiple trials, viral genotypes, treatment regimens, and durations. The sustained virologic response at 12 weeks of follow up was determined to be suitable as a primary endpoint in clinical trials and allows for hepatitis C virus treatment options to be available earlier for patients suffering from this disease. The sustained virologic response at 4 weeks of follow up may have utility in guiding dose and treatment strategies when designing registration trials. The use of earlier time points for key regulatory decisions and dose selection may facilitate drug development for additional therapeutics under investigation.

In addition to identification of additional endpoints for clinical studies, pooled data (both preclinical and clinical) have also been applied to the analysis of safety issues. An analysis of 199 clinical trials of 11 antiepileptic drugs by FDA helped quantify the increased risk of suicidal behavior or ideation for patients and prescribers. (Statistical Review and Evaluation: Antiepileptic Drugs and Suicidality (May 23, 2008): http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsa

ndProviders/UCM192556.pdf.) An independent analysis of data on 5 potential biomarkers of kidney injury by the Predictive Safety Testing Consortium led to their qualification for inclusion in pre-clinical safety data submissions (Ref. 3). These markers are now being evaluated for their utility as more sensitive markers of early kidney damage in human clinical trials. Thus, advances in regulatory science can arise from analysis of diverse data submitted as part of marketing applications, including, for example data related to clinical outcomes, safety, biomarker status, drug disposition, drug action, or patient reported outcomes. (See, e.g., 21 CFR 314.50 (specifying the content of new drug applications).)

FDA has considerable expertise in analyzing individual patient level and aggregated clinical trial data, but recognizes the potential to further advance regulatory science by allowing other experts the opportunity to contribute to these efforts. To fully realize the potential of these data, experts outside of FDA would need to become actively engaged in the research. FDA is considering approaches to providing access by non-FDA experts and other interested parties to data that have research value in a way that would both safeguard the privacy interests of patients enrolled in clinical trials, and appropriately protect the commercial investments of sponsors.

Consistent with and in furtherance of the objectives and mission of Commissioner Hamburg's Transparency Initiative, FDA intends to consider the extent and nature of public availability of de-identified and masked subject level data necessary to achieve specific aims. For more information on the Transparency Initiative, see http://www.fda.gov/AboutFDA/Transparency/TransparencyInitiative/default.htm.

FDA uses the term "masked data" in this notice to refer to data with information removed that could link it to a specific product or application. The Agency will consider different strategies to minimize the ability to identify specific products and the impact of any such

strategies. Such strategies might include making available certain data from a random sample or appropriately chosen subset of subjects, restricting the data fields made available or pooling data where possible from studies of multiple members of a product class, without identifying the specific product.

For the purposes of this notice, de-identified data refers to data that does not identify an individual and with respect to which there is no reasonable basis to believe that the information can be used to identify an individual. Cf. 45 CFR 164.514(a) (although FDA references the standard used in the Privacy Rule here, the Agency notes that it is not a covered entity for the purposes of that Rule). The Agency has an unwavering commitment to protecting the privacy of research subjects' identities. As such, consistent with FDA's regulations at 21 CFR 20.63(a), any data that might be made available under this proposal would be stripped of any information which could identify patients or research subjects, either directly or through combination with other publicly available information. See id. ("The names and other information which would identify patients or research subjects…shall be deleted before the record is made available for public disclosure.") This same regulation also directs outside parties to remove such personal identifiers from records prior to submission to FDA. (See § 20.63(b).)

De-identified and masked data could be used to advance public health. For example, a model of disease progression in control arms of future studies could be based on pooled control group data from past studies of the same disease or indication and would not require identification of a product or even product class nor would there be personal identifiers associated with the data. Similarly, characterization of risk factors might only involve control group data. On the other hand, validating a biomarker as a surrogate for a clinical outcome or as

a predictive classifier of potential treatment response might require identification of products by class or analysis across a class to show consistency.

We note that this proposal contemplates the availability of certain data after appropriate steps have been taken to de-identify it and remove the data's link to a specific product, study, or application. This proposal does not pertain to unmasked safety and effectiveness data, (i.e., data that can be linked to a specific, identified application) including full study reports; the circumstances under which this information is disclosed is already specifically set forth in the Federal Food Drug and Cosmetic Act and FDA's regulations. Further, FDA will not make available business-related confidential commercial information contained in product applications, including but not limited to information concerning licensing agreements and information identifying suppliers, unless such information has already been publicly disclosed by the sponsor. Nor will the Agency make available trade secret information under this proposal. Such information will continue to be treated in a manner consistent with sections 301(j), 505(l), 520(c), 535(d), and 537(e) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 331(j), 351(l), 360j(c), 360ll(d), and 360nn); the Trade Secrets Act (18 U.S.C. 1905); and FDA's regulations (21 CFR 20.61, 314.430, 601.51, and 814.9).

II. Request for Comments

FDA is interested in receiving comments from the public on the following topics: (1) What factors should be considered in masking study data (e.g., data fields from regulatory submissions to remove or modify, number of different products to pool within a product class), (2) what limitations, if any, should there be on the Agency's ability to make available the masked data as described previously, (3) are there any additional factors FDA should consider in de-identifying data in addition to FDA's requirement to remove any names and other information

(e.g., birth date, death date, local geographic information, contact information) which would identify patients or research subjects before disclosing information, (4) would regulatory changes facilitate implementation of such a proposal, and if so, what changes would be most useful, and (5) which situations do you believe disclosing masked data would be most useful to advance public health?

Interested persons may submit either electronic comments regarding this document to http://www.regulations.gov or written comments to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of comments. Identify the question your comment addresses by the number assigned to that question. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at http://www.regulations.gov.

III. References

The following references have been placed on display in the Division of Dockets Management (see ADDRESSES) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday, and are available electronically at http://www.regulations.gov. (FDA has verified all the Web site addresses in this reference section, but we are not responsible for any subsequent changes to the Web sites after this document publishes in the Federal Register.)

1. Hamburg, M. A. and J. M. Sharfstein, "The FDA as a Public Health Agency," New England Journal of Medicine, 2009 June 11; 360(24):2493-5.

2. Chen J., J. Florian, W. Carter, et al. "Earlier Sustained Virologic Response End Points for Regulatory Approval and Dose Selection of Hepatitis C Therapies." Gastroenterology, 2013 March 4 http://www.sciencedirect.com/science/article/pii/S0016508513002886

3. Dieterle, F., et al., "Renal Biomarker Qualification Submission: A Dialog Between the FDA-EMEA and Predictive Safety Testing Consortium," Nature Biotechnology, 2010 May; 28(5):455-62.

Dated: May 29, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

[FR Doc. 2013-13083 Filed 06/03/2013 at 8:45 am; Publication Date: 06/04/2013]